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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,725	04/23/2001	Hans-Werner Heinrich	101195-44	4120

27387 7590 07/12/2006

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EXAMINER	
WILLIAMS, KAREN M	
ART UNIT	**PAPER NUMBER**
PCT	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,725	HEINRICH ET AL.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2005 and 28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendments filed 28 December 2005 and 28 April 2006 are acknowledged and have been entered. Claims 1-18 remain in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The disclosure is objected to because of the following informalities: the specification contains too many grammatical, idiomatic, and spelling errors to list specifically and should be carefully revised. Appropriate correction is required.

Claims 1-11 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, for reasons similar to those of record, that the specification contains subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As set forth previously, applicant teaches only polyclonal antibodies and provides no description or guidance to any monospecific species which functions in the invention. As set forth, adequate written description requires more than a mere statement that a product is part of the invention, more than a reference to a potential method of isolating it, and more than a generic statement which defines a genus of products by only their functional activity. As set forth, the product itself is required as well as recitation of a representative number of products falling

within the scope of a claimed genus. Moreover, as set forth, all possible analogs of a product are not enabled by a disclosure wherein the characteristics of the analogs are unpredictable.

Upon further consideration, the examiner can also find nothing in the disclosure that describes or enables any antibodies or combination of antibodies, including the polyclonal antibodies specifically exemplified, as functional in the invention. The exemplified antibodies bind to the peptides used as immunogens or to elastase in a Western blot after sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). Applicant states that "not every antibody detects all isoforms" in this assay (see page 10), appearing to imply that some antibodies bind all isoforms. However, there is nothing in the specification to indicate which, if any, of the anti-peptide antibodies bind to all isoforms so that one could practice the invention as desired and claimed to detect all isoforms with a single antibody absent further unguided unpredictable experimentation to complete applicant's suggested invention. Applicant also provides no guidance for usable combinations, particularly since some of the peptides suggested for use by applicant would be expected to elicit antibodies that bind to an isoform which corresponds to porcine elastase and which is not expressed in the human pancreas (see e.g. Tani et al., page 1231, and Fig. 9), and detection of a protein having epitopes recognized by combinations containing such antibodies would unquestionably complicate the assay in any patient receiving enzyme replacement therapy with animal, such as porcine, pancreatic enzymes (see Schneider et al. in this regard). Further, applicant does not teach combinations usable together and one would not be able to perform a sandwich assay with combinations that do not bind to epitopes found at two sites on the same enzyme molecule, e.g. a combination would not function in the invention in which one antibody binds elastase I as known to the art and the other

binds to an epitope on the un-expressed isoform which does not cross-react with elastase I, combinations suggested by applicant's disclosure. Moreover, there is nothing that describes or enables any antibodies capable of predictable binding to any or all of the elastase enzyme isoforms as found in stool or body fluid samples, because only binding to proteins in Western blots, i.e. after SDS denaturation, is specifically exemplified. One could not predict the ability of any of the antibodies to the suggested peptides to bind to non-denatured protein as found in a fluid sample from a patient. Absent further written description and guidance from applicant, one would have no assurance of successfully obtaining appropriate functional reagents and predictably performing the method as suggested by applicant.

Further, applicant does not teach other than immunoassays for the determination. Alternative assays to quantitate all isoforms of the enzyme, such as enzymatic activity assays, are not known to the art due to lack of sufficient sensitivity and the presence of protease inhibitors, among other complications (see Geokas et al.).

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." The court further stated that: "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill

of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

Applicant's arguments filed 28 December 2005 have been fully considered but they are not deemed to be persuasive. Applicant urges that disclosure of methods to make antibodies adequately describe and enable the invention as claimed and that the common structure of antibodies inform one as to what structure is important for function. This is not found persuasive for the reasons set forth previously and above regarding definition of a genus merely by function. Notwithstanding applicant's assertions to the contrary, knowledge of common antibody structure does not guide one to the structure (sequence) of the complementarity determining regions of any antibody functional in the invention, the sequences which primarily define the specificity of any particular antibody. Thus applicant has set forth no structure-function correlation to describe the genus of antibodies encompassed by the claims. The state of the art is such that one cannot readily envision antibody structures which bind or do not bind the peptides suggested for use by applicant. Applicant urges that the invention relates to heterogeneous populations of different antibodies. This is not found persuasive because single antibodies and monoclonal antibodies are instantly claimed.

Claims 1-18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 and 16 involve method claims and, as such, they should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing,

reacting, and detecting. "Employing" or "using" are not valid method steps. These claims are indefinite because without active, positive steps delimiting how the method is actually practiced it is unclear what method/process applicant is intending to encompass. The claims should also clearly state each component used in the method and the relationship of the various components, and should not be a mere cataloging of parts.

In claims 1-6, "the serum, secretions, or excretions" lack antecedent basis.

In claims 2-4, recitations of "the amino-acid sequence" lack antecedent basis. It is not clear what applicant intends as excluded because the excluded amino acid sequence is of a peptide not an iso-enzyme.

In claims 3-4, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

Claim 4 fails to end with a period. It is believed that --antigens-- rather than "antigenes" was intended at line 2. At line 3, --immunization-- rather than "the antigens" should be inserted.

In claim 5, "the antibodies" lack antecedent basis.

Claim 6 is of improper dependent form for failing to further limit the subject matter of a previous claim.

In claim 7 and claims dependent thereupon, it is not clear how one determines what is "standard" and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In these claims, incorrect "SEQ ID NO:" identifiers are recited.

In claim 8, it is not clear how one determines what is "suitable" and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 10, 11, and 16 are of improper dependent form for failing to further limit the subject matter of a previous claim.

In claims 12-15, incorrect "SEQ ID NO:" identifiers are recited.

Claims 17 and 18 are indefinite in that the claims set forth an intended use but fail to point out what components are included or excluded by the claim language. In these claims, "the diagnosis" lacks antecedent basis.

Applicant's arguments filed 28 December 2005 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

Claims 1-8 and 10-18 are rejected under 35 U.S.C. § 102(b) as being anticipated by Scheefers et al. (U.S. Pat. No. 5,622,837) in light of the instant disclosure for reasons of record.

Claims 1-8, 10, and 12-18 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sziegoleit et al. (Clin. Biochem. 22: 79, 1989) in light of the instant disclosure for reasons of record.

Applicant's arguments filed 28 December 2005 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, Scheefers et al. clearly teach elicitation of both polyclonal and monoclonal antibodies to purified enzyme, not only to the peptide disclosed in the reference. And, as is noted by applicant, the excluded sequence is not found in the purified enzyme. Applicant urges that no isoform is mentioned in the reference of Sziegoleit et al. This is not found persuasive because the enzyme isolated from

multiple organs by the references of Sziegoleit et al. or Scheefers et al. would inherently be a mixture of the elastase I isoforms (i.e. elastases IIIA and IIIB), and polyclonal antibodies elicited thereto would inherently bind to the isoforms and cross-react with similar epitopes as found in elastase II. Further, the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)).

The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Tani et al. (J. Biol. Chem. 263: 1231, 1988) teach the sequences of human elastase genes (see Fig. 9). The reference teaches that the sequence identified therein as elastase I is not expressed in human adult pancreas (see page 1231, col. 2) and that the sequences identified therein as elastase III are human elastase I as known to the art (see page 1237, col. 2).

Geokas et al. (J. Biol. Chem. 252: 61, 1977) teach an immunoassay for human elastase II in human serum and the elevation of the enzyme therein in individuals with acute pancreatic inflammation (see paged 66, col. 2).

Schneider et al. (Clin. Chem. 51: 1052, 2005) teach complications if antibodies in a human elastase detection assay bind to porcine elastases.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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July 3, 2006

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